# The effect of medical clowning on pregnancy rates after in vitro fertilization and embryo transfer (IVF-ET)

This experimental prospective quasi-randomized study examining the impact of a medical clowning encounter after ET after IVF found that the pregnancy rate in the intervention group was 36.4%, compared with 20.2% in the control group (adjusted odds ratio, 2.67; 95% confidence interval, 1.36–5.24). Medical clowning as an adjunct to IVF-ET may have a beneficial effect on pregnancy rates and deserves further investigation. (Fertil Steril® 2011;■:■–■. ©2011 by American Society for Reproductive Medicine.)

**Key Words:** In vitro fertilization, medical clowning, pregnancy rate

Infertility and treatment by IVF-ET have been associated with stress (1–4). Stress reduction might improve fertility (5). The beneficial effect of humor in stress situations is well established (6–10). Humor and laughter may have an effect on the embryo-uterine interplay through neuroendocrine pathways or nonovarian stress reduction, augmenting uterine receptivity (11–23). Medical clowning uses humor as an adjunct therapeutic tool. However, it has not been explored in the context of IVF. The aim of this study was to evaluate the impact of medical clowning on pregnancy rates after IVF-ET.

Patients undergoing ET at Assaf Harofeh Medical Center's IVF Unit from June 1, 2005, to May 31, 2006, were recruited. During this period, a medical clown visited the unit approximately every second week. The original design was an experimental prospective quasi-randomized study, recruiting all women attending the unit for ET on the clown's visit day to the intervention group and all who were invited for ET on another day of the same week to the control group. All women who attended the unit during a clown's visit day were indeed recruited to the intervention group, but controls were not always recruited on the corresponding "nonclown" days. Therefore, in the end there were fewer days of recruitment to the control than to the intervention group. To compensate, we identified from medical records nonrecruited women who had attended the unit on nonclown days and supplemented the control group. The final design was a quasi-randomized trial with supplementary controls from the same population.

A structured questionnaire (including demographic and clinical information), was completed for all women on the day of the ET (or from the medical records for the 25 women supplemented to the control group). The outcome of just one treatment cycle per woman was evaluated. Determination of pregnancy required ultrasound demonstration of a gestational sac.

Informed consent was obtained from all participants on the day of ET. Only three women refused participation. The study was approved by the center's Institutional Review Board (no. 114/05).

Patients included in the study were treated by routine controlled ovarian hyperstimulation (COH) protocols for IVF using a long GnRH agonist or GnRH antagonist, as described elsewhere (24).

Oocytes were retrieved by ultrasound-guided transvaginal follicular aspiration, 35–38 hours after administration of 5,000 IU hCG. Fertilization was assessed 16–18 hours after routine IVF or intracytoplasmic sperm injection (ICSI) and after the presence of two pronuclei was recorded. Embryonic cleavage and morphologic appearance were assessed 40–44 hours and 64–68 hours after ICSI/IVF. A morphologic score was given for each embryo according to degree of fragmentation: 1, no fragmentation; 2, <20% fragmentation; 3, 20%–50% fragmentation; 4, >50% fragmentation.

ET was performed using a Wallace catheter (Marlow Technologies, Willoughby, OH). The number of embryos to be transferred was decided according to the Israeli Ministry of Health guidelines, that is, only two embryos for the first three ETs. A third embryo is allowed for women aged >35 years, and a fourth for women aged

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≥40 years or in cases after repeated implantation failure. All patients (in both the intervention and control groups) received the same information regarding the quality and number ET.

Luteal support using micronized P was given to all patients, starting on the day of ET, until serum β-hCG measurement 14 days later, and continued until the eighth week of gestation in pregnant patients.

Each patient in the intervention group was visited by a professional medical clown immediately after ET, while lying in bed. This encounter lasted 12–15 minutes and included a routine developed by the principal investigators (SF and AS) as suitable for such patients. The routine included jokes, tricks, and magic and was performed on a one-to-one basis with the clown dressed as a "chef de cuisine." The same clown performed the same routine at all visits.

Given a two-sided significance level of .05 and a difference of 15% in the clinical pregnancy rate between the two groups, the group size needed for 80% statistical power was 94 patients in each arm.

Statistical analysis was performed using the $\chi^2$ test for comparison of the groups' pregnancy rates and other categorical variables, and Student's two-sided *t* test regarding continuous variables. A multivariable logistic regression model was used to adjust the pregnancy rates for prognostic factor imbalances. $P<.05$ was considered statistically significant.

The study sample included 219 patients (110 in the intervention group and 109 in the control group). There were no significant differences between the groups regarding age (mean age, 34.2 ± 4.9 and 34.1 ± 5.4 years, respectively), education (mean years, 14.3 ± 2.8 and 14.3 ± 2.3, respectively), religious affiliation, or family status. Women in the intervention group had similar rates of irregular menses, types of infertility, and previous IVF cycles compared to the control group. Women in the intervention group had significantly more years of infertility (4.1 ± 2.9 and 3.4 ± 2.8 years, respectively). No significant differences were observed in the type of ET (fresh vs. frozen), levels of peak $E_2$, type of COH protocol, type of cycle, number of retrieved oocytes, fertilized oocytes, or ET. More women in the control group had ET on day 3, while more in the intervention group had ET on day 2 ($P=.06$).

The pregnancy rate in the intervention group was 36.4%, compared with 20.2% in controls ($P=.008$). In multivariable analysis (Table 1), the intervention group had a 2.67 (95% confidence interval [CI], 1.36–5.24) higher odds of pregnancy than controls after adjustment for age, diagnosis and type of infertility, length of infertility, cycle characteristics, number of ETs, and ET day.

## TABLE 1

**Multivariable logistic regression analysis model for pregnancy rates after IVF-ET adjusted for study group, age, infertility, and cycle characteristics.**

| Characteristic | N | Pregnancy, n (%) | *P* value | Adjusted odds ratio (95% CI) | *P* value |
|---|---|---|---|---|---|
| Group | | | .008 | | .004 |
| Control | 109 | 22 (20.2) | | 1.0 | |
| Intervention | 110 | 40 (36.4) | | 2.67 (1.36–5.24) | |
| Age, y | | | .45 | | .54 |
| <30 | 55 | 16 (29.1) | | 1.0 | |
| 30–34 | 65 | 22 (33.8) | | 1.25 (0.53–2.92) | |
| 35–39 | 62 | 17 (27.4) | | 0.77 (0.30–1.95) | |
| 40–46 | 37 | 7 (18.9) | | 0.58 (0.17–1.95) | |
| Diagnosis of infertility | | | .44 | | .87 |
| Hormonal | 20 | 4 (20.0) | | 0.89 (0.26–3.12) | |
| Mechanical | 30 | 7 (23.3) | | 0.78 (0.28–2.13) | |
| Male | 130 | 39 (30.0) | | 1.0 | |
| Unexplained | 38 | 11 (28.9) | | 1.27 (0.53–3.02) | |
| Type of infertility | | | .69 | | .44 |
| Primary | 100 | 27 (27.0) | | 1.0 | |
| Secondary | 119 | 35 (29.4) | | 1.30 (0.67–2.52) | |
| Type of cycle | | | .19 | | .24 |
| Fresh | 187 | 56 (29.9) | | 1.0 | |
| Frozen | 32 | 6 (18.7) | | 0.51 (0.17–1.56) | |
| No. of transferred embryos | | | .30 | | .97 |
| 1–2 | 133 | 41 (30.8) | | 1.0 | |
| 3–4 | 86 | 21 (24.4) | | 1.01 (0.47–2.16) | |
| Length of infertility, y | | | .27 | | .14 |
| 1–2 | 83 | 27 (32.5) | | 1.0 | |
| 3–4 | 64 | 16 (25.0) | | 0.53 (0.23–1.19) | |
| 5+ | 54 | 11 (20.4) | | 0.45 (0.18–1.13) | |
| Transfer day | | | .79 | | .27 |
| 2 | 141 | 40 (28.4) | | 1.0 | |
| 3–5 | 73 | 22 (30.1) | | 1.48 (0.74–2.97) | |

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The concept of humor or laughter being therapeutic appears in many ancient cultures, but it has not been evaluated using evidence-based methodology. Studies by Fry (11–16), Cousins (17), and Berk et al. (18–23) have laid the foundations for investigating various physiological parameters influenced by laughter. Based on research in psychoneuroimmunology, it appears that increased stress levels can lead to changes in psychological and physiological functioning and in the levels of stress hormones. Other messengers such as PRL, growth hormone, insulin, glucagon, thyroid hormone, and gonadotropin can also be affected by stress (25), as may levels of neurotransmitters, neurohormones, cytokines, and various cells in the immune system (26). Humor and laughter are believed to act as a coping mechanism to reduce stress and psychological symptoms related to negative life events and improve quality of life and immune function (7–10, 27, 28).

Interactions between hormonal and neurobiological systems may affect reproductive processes (29). Reciprocal interference is even more plausible, since stress and reproduction are controlled by similar nuclei within the hypothalamus and by similar neurotransmitters. An association between activated T-cell lymphocytes in the peripheral blood and implantation rates has been suggested in women undergoing IVF (30–33).

Although the exact mechanism whereby stress interferes with reproductive processes is not fully understood, experimental evidence (34–36) increasingly indicates that lower stress levels result in better fertility treatment outcome (37–40). Recently, a mouse implantation model, on the possible impact of stress on uterine receptivity, independent of hypophysial-pituitary-gonadal axis dysfunction (41), revealed that mice exposed to stress had significantly fewer implantation sites. There is substantial initial evidence that psychological disposition influences fertility and thus the outcome of fertilization techniques (5). However, most publications in this field are empiric and lack rigorous methodology (42, 43).

The current results suggest that medical clowning, used as an adjunctive intervention, may have a beneficial effect upon IVF-ET outcome. The results are surprising since the patients in the intervention group were visited by the clown for only 12–15 minutes. This is in disagreement with previous publications indicating that the most successful interventions have strong education and skills training components and require much longer periods of intervention (34, 44).

Allocation of the intervention was quasi-randomized. While we are unaware of confounding variables that could explain the observed difference in pregnancy rates, we cannot completely rule them out. Women in the intervention group had a higher pregnancy rate, despite having more years of infertility (which was accounted for in the multivariable model). Boivin et al. (45) observed that less stressed infertile patients do not feel they need psychological intervention. It is possible that stress-reducing techniques are more useful for those experiencing more stress resulting from a longer duration of infertility. Individual baseline personality differences such as anxiety and coping strategies were beyond the scope of the present analysis. These characteristics may influence the reaction to the clown's visit and affect the pregnancy rates. Embryo morphology was not compared between the groups and could have had an impact on outcome. Although this study presents results from a single IVF unit, the population is nonselective since the national insurance policy in Israel covers all IVF for all women for the first and second child.

The resources required to implement medical clowning are far less than those for other stress-reducing techniques. Moreover, the simple nature of a medical clown encounter makes it feasible for implementation in other settings and cultures. In view of the positive results observed in this study, the use of humor and medical clowning as an adjunct to treatment for infertility deserves further investigation.

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